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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,034	10/11/2001	Kin-Ming Lo	LEX-009DV	4315
21323	7590	06/29/2004	EXAMINER	
TESTA, HURWITZ & THIBEAULT, LLP HIGH STREET TOWER 125 HIGH STREET BOSTON, MA 02110			JIANG, DONG	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/977,034

Applicant(s)

LO ET AL.

Examiner

Dong Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26,27,34,35,37 and 38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26,27,34,35,37 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED OFFICE ACTION

The request filed on 06 April 2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/977034 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 06 April 2004 is acknowledged and entered. Following the amendment, claims 28-33 and 36 are canceled, and claims 26 and 27 are amended.

Currently, claims 26, 27, 34, 35, 37 and 38 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 28-33 and 36 are moot as the applicant has canceled the claims.

The new matter rejection of claims 26, 27, 34, 35, 37 and 38, under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's argument and the specification.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26, 27, 34, 35, 37 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is indefinite because, instead of specifying the structural arrangement/orientation of the fusion protein and the Fc portion, the newly added limitations of "targeting an Fc fusion protein ... to a liver tissue, while reducing an effect of an Fc effector function" and "providing the immunoglobulin Fc region in an orientation that reduces the effect of an Fc effector function" describe the orientation of the Fc fusion protein by its effect. As such, the metes and bounds of the fusion protein, and hence the claim cannot be determined. Applicants have indicated in the interview on 15 March 2004 that the current invention is based on the specific orientation of the

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Fc portion in the fusion protein. However, the presently amended claim does not reflect such as the new functional limitation does not make it clear as to what is the orientation of the Fc in the fusion protein, and thus, the claim does not particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 is similarly indefinite.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 34, 35, and 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, taken with Lo et al., US 5,541,087, for the reasons of record set forth in the previous Office Actions, mailed on 05 May 2003, and on 29 January 2004.

Applicants argument filed on 06 April 2004 has been fully considered, but is not deemed persuasive for reasons below.

At page 5 of the response, the applicant argues that the invention is based in part on the discovery that the N- to C-terminal orientation of the Fc-IFN- α fusion protein impairs antibody-dependent cell mediated cytotoxicity (ADCC) and complement fixation, but maintains preferential targeting to liver tissues, which has not been taught or suggested prior to applicants

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invention, that none of the Chang, Lo or Capon teaches or suggests methods of targeting an Fc-IFN- α fusion pro to a liver tissue while reducing an effect of an Fc effector function, nor that the N- to C-terminal orientation of the Fc-IFN- α fusion protein has any impact on effector function, and any reasonable expectation of targeting an Fc-IFN- α with reduced effector function to a liver tissue by administering a fusion protein having a specific N- to C-terminal orientation. This argument is not persuasive for the following reasons. With respect to the specific orientation of the fusion molecule, it is Examiner's understanding from the interview that applicants indicated that the present invention is based on the specific orientation of the Fc portion, not the N- to C-terminal arrangement of the Fc-IFN- α fusion, which has been indicated by the prior art (see the prior art rejection in the previous Office Action, paper No. 7, mailed on 05 May 2003, at pages 3-4). The present claims, as amended, do not indicate the orientation of the Fc portion within the molecule. As such, it is still obvious over the prior art teachings for the same reasons set forth in the previous Office Action, paper No. 7. As to "targeting an Fc-IFN- α fusion protein to a liver tissue while reducing an effect of an Fc effector function", since the method of treatment using the Fc-IFN- α fusion protein is obvious over the prior art, and liver tissue expresses Fc receptor, it would be an inherent property of the fusion molecule to target liver tissue and to reduce an effect of an Fc effector function when it is used for treatment, which does not cause the claims drawn to those things to distinguish over prior art.

With respect to reasonable expectation of targeting an Fc-IFN- α with reduced effector function to a liver tissue, once again, it would be an inherent property of the fusion molecule, and it would happen when the same molecule is used for the treatment regardless whether one would expect it or not.

Further, *even if* the present claims made it clear as to the specific orientation of the Fc portion of the fusion molecule, for example, the fusion orientation of molecule is Fc(CH₂-CH₃)-IFN- α (as opposed to Fc(CH₃-CH₂)-IFN- α), they are still obvious over the prior art because Lo teaches such a type of fusion proteins. Lo teaches a DNA of general applicability for production and secretion of fusion proteins, which comprises a polynucleotide encoding a secretion cassette, "immunofusin", as it has a N-terminal Fc and a target protein, wherein the secretion cassette can be fused to various target proteins (column 2, lines 11-24). Further Lo teaches that the Fc γ

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region is comprised of three subregions: a hinge region, a CH2, and a CH3, that attached to the 3' end of the DNA encoding the secretion cassette is a DNA encoding the target protein, and that optionally, DNA encoding a proteolytic cleavage site can be interposed between the DNA encoding the CH3 and the DNA encoding the target protein (column 5, lines 11-17, and Figure 1), indicating the orientation/arrangement of the fusion molecule is Fc(CH2-CH3)-X (target protein), which is the same as that of the present invention.

Claims 27 and 37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, and Lo et al., US5,541,087, as applied to claims 26, 28-30, 34-36 and 38 above, and further in view of Capon et al., US5,116,964, for the reasons of record set forth in the previous Office Actions, mailed on 05 May 2003, and on 29 January 2004.

Applicants argument filed on 06 April 2004 has been fully considered, but is not deemed persuasive for the same reasons above as the traversal is based on the same ground for the rejection above.

Conclusion:

No claim is allowed.

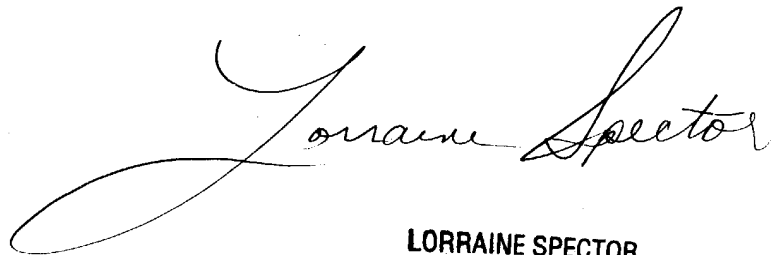
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Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

A handwritten signature in cursive script that reads "Lorraine Spector". The signature is written in dark ink and is positioned above the printed name and title.

**LORRAINE SPECTOR
PRIMARY EXAMINER**

Dong Jiang, Ph.D.
Patent Examiner
AU1646
6/15/04